

CLAIMS

We claim:

1. A system comprising a closed system synthesizer configured for parallel synthesis of three or more polymers.

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2. The system of Claim 1, wherein said three or more polymers comprise ten or more polymers.

3. The system of Claim 2, wherein said ten or more polymers comprise 48 or
10 more polymers.

4. The system of Claim 3, wherein said 48 or more polymers comprise 96 or more polymers.

5. The system of Claim 1, wherein said polymers comprise nucleic acid
15 polymers.

6. The system of Claim 5, wherein said nucleic acid polymers comprise
20 DNA.

7. The system of Claim 6, wherein said DNA comprises oligonucleotides.

8. The system of Claim 1, wherein said polymers comprise three or more
25 distinct oligonucleotides.

9. The system of Claim 8, wherein said polymers comprise twenty or more
distinct oligonucleotides.

10. The system of Claim 9, wherein said polymers comprise fifty or more
30 distinct oligonucleotides.

11. The system of Claim 1, wherein said synthesizer is configured to produce 200 or more polymers per day.

12. The system of Claim 11, wherein said synthesizer is configured to produce 1000 or more polymers per day.

13. The system of Claim 12, wherein said synthesizer is configured to produce 2000 or more polymers per day.

14. The system of Claim 11, wherein said polymers comprise oligonucleotides.

15. The system of Claim 11, wherein said oligonucleotides have 20 or more bases.

16. The system of Claim 15, wherein said oligonucleotides are produced at a 1 μ mole scale.

17. The system of Claim 15, wherein said oligonucleotides are produced at less than a 1 nmole scale.

18. A synthesizer comprising:

- a. a reaction support comprising three or more reaction chambers; and
- b. a plurality of reagent dispensers configured to simultaneously form closed fluidic connections with each of said reaction chambers, wherein said reagent dispensers are each configured to deliver all reagents necessary for a polymer synthesis reaction.

19. The synthesizer of Claim 18, wherein said reaction support comprises 50 or more reaction chambers.

20. The synthesizer of Claim 18, wherein said reaction support comprises 96 or more reaction chambers.

21. The synthesizer of Claim 18, wherein said reaction chambers comprise
5 synthesis columns.

22. The synthesizer of Claim 21, wherein said synthesis columns comprise nucleic acid synthesis columns.

10 23. The synthesizer of Claim 18, wherein said reagent dispensers are fluidically connected to a plurality of reagent tanks.

24. The synthesizer of Claim 23, wherein said reagent dispensers are connected to said plurality of reagent tanks through a plurality of channels.

15 25. The synthesizer of Claim 23, wherein said plurality of reagent tanks comprise one or more tanks selected from the group consisting of acetonitrile tanks, phosphoramidite tanks, argon gas tanks, oxidizer tanks, tetrazole tanks, and capping solution tanks.

20 26. The synthesizer of Claim 23, wherein said reaction support comprises a fixed reaction support.

25 27. The synthesizer of Claim 23, wherein said reaction support further comprises a plurality of waste channels, said waste channels in closed fluidic contact with each of said reaction chambers.

28. The synthesizer of Claim 27, further comprising a detection component, wherein said detection component detects detritylation.

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29. The synthesizer of Claim 28, wherein said detection component comprises a CCD camera.

5 30. The synthesizer of Claim 28, wherein said detection component comprises a spectrophotometer.

31. The synthesizer of Claim 28, wherein said detection component comprises a conductivity meter.

10 32. The synthesizer of Claim 18, further comprising a heating component.

33. The synthesizer of Claim 18, further comprising a mixing component.

15 34. A synthesizer comprising:
a. a fixed reaction support comprising three or more reaction chambers;
and
b. a plurality of reagent dispensers configured to simultaneously form closed fluidic connections with each of said reaction chambers.

20 35. A nucleic acid synthesizer configured to produce 200 or more oligonucleotide per day.

36. The synthesizer of Claim 35, configured to produce 1000 or more oligonucleotides per day.

25 37. The synthesizer of Claim 35, configured to produce 2000 or more oligonucleotides per day.

38. The synthesizer of Claim 35, wherein said oligonucleotides comprise 20
30 or more bases.

39. The synthesizer of Claim 38, wherein said oligonucleotides comprise 40 or more bases.

5 40. The synthesizer of Claim 35, wherein said oligonucleotides are produced at a 1 μ mole or greater scale.

41. The synthesizer of Claim 35, wherein said oligonucleotides are produced at a 1 nmole or smaller scale.

10 42. The synthesizer of Claim 35, wherein each of said 200 or more oligonucleotides comprises a different sequence.

15 43. A system comprising a processor, wherein said processor is configured to operate a closed system nucleic acid synthesizer for parallel synthesis of three or more nucleic acid molecules.

44. A system comprising a processor, wherein said processor is configured to operate a nucleic synthesizer and a cleavage and deprotect component.

20 45. The system of Claim 44, further comprising a computer memory, said computer memory comprising nucleic acid sample order information.

25 46. The system of Claim 45, wherein said computer memory further comprises allele frequency information.

47. The system of Claim 45, wherein said computer memory further comprises disease association information.

30 48. The system of Claim 1, further comprising a fail-safe reagent delivery component for delivery of one or more reagents to said solid phase synthesizer.

49. The synthesizer of Claim 18, further comprising a fail-safe reagent delivery system for delivery of one or more reagents from said reagent dispensers.

50. The solid phase synthesizer of Claim 34 further comprising a fail-safe reagent delivery system for delivery of one or more reagents from said reagent dispensers.

51. The synthesizer of Claim 35 further comprising a fail-safe reagent delivery system for delivery of one or more reagents so said synthesizer

52. The system of Claim 44 further comprising a fail-safe reagent delivery system for delivering one or more reagents to said nucleic synthesizer.

53. A system comprising a substantially closed system synthesizer configured for parallel synthesis of three or more polymers.

54. The system of Claim 1, further comprising a heating component providing substantially uniform heat during said parallel synthesis.

55. The system of Claim 54, wherein said closed system synthesizer is under controlled pressure.

56. The system of Claim 54, wherein said heating component comprises delivery of heated reagents.

57. The synthesizer of Claim 18 further comprising a heating component providing substantially uniform heat to at least two of said three or more reaction chambers.

58. The synthesizer of Claim 57, wherein said heating component comprises delivery of heated reagents to said at least two of said three or more reaction chambers.

59. The synthesizer of Claim 34, further comprising a heating component providing substantially uniform heat to at least two of said three or more reaction chambers.

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60. The synthesizer of Claim 59, wherein said heating component comprises delivery of heated reagents to said at least two of said three or more reaction chambers.

61. The synthesizer of Claim 35, further comprising a heating component providing substantially uniform heat during the production of said 200 or more oligonucleotides.

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62. The system of Claim 44, further comprising a heating component for providing substantially uniform heat to reaction chambers of said nucleic synthesizer, said heating element being operated by said one or more processors.

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63. The system of Claim 54, wherein said heating component provides an optimized reaction temperature for a coupling step, said optimized reaction temperature being in the range of about 20 degrees C to about 60 degrees C.

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64. The synthesizer of Claim 57, wherein said heating component provides an optimized reaction temperature for a coupling step, said optimized reaction temperature being in the range of about 20 degrees C to about 60 degrees C.

65. The synthesizer of Claim 59, wherein said heating component provides an optimized reaction temperature for a coupling step, said optimized reaction temperature being in the range of about 20 degrees C to about 60 degrees C.

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66. The synthesizer of Claim 61, wherein said heating component provides an optimized reaction temperature for a coupling step, said optimized reaction temperature being in the range of about 20 degrees C to about 60 degrees C.

67. The system of Claim 62, wherein said heating component provides an optimized reaction temperature for a coupling step, said optimized reaction temperature being in the range of about 20 degrees C to about 60 degrees C.

5 68. The system of Claim 63, further comprising a mixing component.

69. The synthesizer of Claim 64, further comprising a mixing component.

70. The synthesizer of Claim 65, further comprising a mixing component.

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71. The synthesizer of Claim 66, further comprising a mixing component.

72. The system of Claim 67, further comprising a mixing component.

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73. The system of Claims 68 or 72, wherein said mixing component is selected from the group consisting of an ultrasonic mixer, a magnetic mixer, a fluid oscillator, and a vibrational mixer.

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74. The synthesizer of Claims 69, 70 or 71, wherein said mixing component is selected from the group consisting of an ultrasonic mixer, a magnetic mixer, a fluid oscillator, and a vibrational mixer.

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75. The system of Claim 1, further comprising a reagent delivery system external to said closed system synthesizer, wherein said reagent delivery system delivers one or more reagents to said closed system solid phase synthesizer.

76. The system of Claim 75, wherein said reagent delivery system further comprises at least one large volume container comprising a reagent.

77. The system of Claim 75 wherein said reagent delivery system further comprises a plurality of large volume containers, each said large volume container comprising at least one of said reagents.

5 78. The system of Claim 69 in which said large volume containers store in the range of about 2 liters to about 200 liters of one or more reagents.

79. The synthesizer of Claim 18, further comprising, in combination, a reagent delivery system external to said solid phase synthesizer, in which said reagent delivery
10 system delivers one or more reagents to said solid phase synthesizer.

80. The synthesizer of Claim 79, wherein said reagent delivery system further comprises at least one large volume container comprising a reagent.

15 81. The synthesizer of Claim 79, wherein said reagent delivery system further comprises a plurality of large volume containers, each said large volume container comprising at least one of said reagents.

82. The synthesizer of Claim 81, wherein said large volume containers store in
20 the range of about 2 liters to about 200 liters of one or more reagents.

83. The synthesizer of Claim 18, wherein said reagent dispensers are external to said closed system solid phase synthesizer.

25 84. The system of Claim 83, wherein said reagent dispensers are large volume reagent dispensers.

85 The system of Claim 84, wherein said large volume reagent dispensers store in the range of about 2 liters to about 200 liters of one or more reagents.

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85. The synthesizer of Claim 35, further comprising a plurality of large volume reagent dispensers.

86. The synthesizer of Claim 85, wherein said plurality of large volume reagent dispensers are external to said synthesizer.

87. The synthesizer of Claim 86, wherein said large volume reagent dispensers store in the range of about 2 liters to about 200 liters of one or more reagents.

88. The system of Claim 43, further comprising a plurality of large volume dispensers external to said nucleic synthesizer, wherein said processor optionally regulates delivery of a reagent from said large volume dispensers.

89. The system of Claim 44, further comprising a plurality of large volume dispensers, wherein said processor optionally regulates delivery of a reagent from said large volume dispensers to said nucleic synthesizer.

90. The system of Claim 89, wherein said large volume reagent dispensers store in the range of about 2 liters to about 200 liters of one or more reagents.

91. A system comprising a substantially closed system solid phase synthesizer configured for parallel synthesis of three or more polymers; and, a fail-safe reagent delivery system for delivery of a plurality of reagents from large volume reagent delivery systems to said solid phase synthesizer.

92. The system of Claim 91, wherein said large volume reagent delivery systems are external to said solid phase synthesizer.

93. The system of Claim 92, further comprising a closed waste disposal system.

94. The system of Claim 91, further comprising one or more heaters for providing substantially uniform heat for said parallel synthesis.

95. The system of Claim 94, further comprising one or more mixers for
5 mixing said three or more polymers.